DETAILED ACTION

Claims 1-12 are pending in the application. Claims 1-4 are allowed. Claims 5-12 are rejected.

Response to Amendment

Applicant's amendments to claims 1-4 have placed claims 1-4 in condition for allowance; however, a new matter issue, which was created for claim 1 upon addition of the limitations "pyridine-2-yloxy" and "adamantly" still exists for claim 5, which still contains these limitations. See 112 1st paragraph rejection of claims 5-11, below. It is suggested that Applicant amend claim 5 to reflect the scope of claim 1.

Applicant has amended claim 12 to recite a "composition for modulation the activities of peroxisome proliferator activated receptor gamma sub type...". In the interview on October 6th, 2009, the Examiner suggested that claim 12 be amended to recite "a composition for "activating the peroxisome proliferator activated receptor gamma subtype (PPAR γ)". Applicant has retained the use of the term modulating; however, the Examiner does not find that the instant specification is enabled for such claim language. See 112 1st paragraph rejection of claim 12, below.

Claim Objections

Claims 5-11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is suggested that Applicant amend claim 5 to reflect the scope of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the instant claims have been amended to provide for R4, R5, R6 and R7 to be pyridine-2-yloxy and amended to provide for Re to be adamantly.

This subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims which change the scope relative to the originally filed claims may lack written description, see *In re Ruschig*, 371 F.2d 990, 154 USPQ 118 (CCPA) 1967) which supports that the original disclosure of a large genus did not support a later filed claim to a previously unnamed single species. Furthermore, *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir.2000) notes that with respect to *In re Ruschig*, that "Ruschig makes clear that one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say "here is my

invention". In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure."

The only written description in Applicants' originally filed disclosure is for the genus of claims 5-11 wherein R4-R7 and Re have the definitions as originally filed on page 3 of the instant specification. The specific species of No. 24 on page 17 and No. 90 on page 26 only provide support for themselves and not for an amendment to the broad genus that only limits certain variables while not limiting other variables.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition for activating the peroxisome proliferator activated receptor gamma subtype (PPAR γ), does not reasonably provide enablement for a pharmaceutical composition for modulating the activities of peroxisome proliferator activated receptor gamma sub type. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is *undue*. These factors include, but are not limited to: (a) breadth of the claims; (b) nature of the invention; (c) state of the prior art; (d) level of one of ordinary skill in the art; (e) level of predictability in the art; (f) amount of direction provided by the inventor; (g) existence of working examples; and (h) quantity of experimentation needed to make or use the

invention based on the content of the disclosure. (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The above factors, regarding the present invention, are summarized as follows:

(a) *Breadth of the claims* - MPEP 2111.01 states:

> *[T]he words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); Chef America, Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004).*

Accordingly, since Applicant has not given the term "modulating" a special definition in the instant specification, the term is given its' plain meaning. A modulatory binding site is topographically distinct from the orthosteric binding site or active site of the enzyme. Therefore, a modulator binds at a site distinct from the active site and its' effects are through allosteric regulation. Therefore, the instant claims are drawn a pharmaceutical compositions for changing the activity of PPARγ through allosteric modulation. Furthermore, the breadth of the claims is drawn to activation as well as inhibition.

(b) *Nature of the invention* - The nature of the invention is drawn to pharmaceutical compositions containing indene derivatives for use in treating, for instance, diabetes as well as other diseases responsive to changes in PPARγ activity.

(c) *State of the prior art* - The state of the art has not advanced to recognize that indene derivatives having similar structures to those instantly claimed are truly allosteric regulators of PPARγ. Ahn et al. (J. Med. Chem. 2006, 49, 4781-4784) teach that indene derivatives having similar structures bind to the active site of PPARγ. See Figure 1, page 4783. Applicant has not provided any tests or assays that indicate that the instant compounds have a different binding mode than those taught by Ahn et al.

(d) *Level of one of ordinary skill in the art* - The artisans utilizing applicant's compositions would be a collaborative team of synthetic chemists and/or health practitioners, possessing commensurate degree level and/or skill in the art, as well as several years of professional experience.

(e) *Level of predictability in the art* - There is no predictability in the art as to whether a given compound, which possesses the ability to activate/inhibit an enzyme, acts as an orthosteric ligand or allosteric modulator absent a comparison with known compounds that

have been demonstrated to have a particular mode of action. As discussed in section (c), the compounds closest in structure to the instantly claimed compounds have been demonstrated to bind at the active site of PPARγ. Therefore, the level of predictability is low in determining which, if any, of the instant compounds would bind to an allosteric site of PPARγ.

(f) *Amount of direction provided by the inventor* - The application is negligent regarding direction with respect to making and using compositions for modulating the activities of peroxisome proliferator activated receptor gamma sub type. Applicant has only provided assay data that demonstrates that the instantly claimed compounds activate PPARγ. There is no direction or teaching that suggests that the instant compounds are capable of modulating the activites of PPARγ.

(h) *Quantity of experimentation needed to make or use the invention based on the content of the disclosure* - Predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation (Jordan, V. C. *Nature Reviews: Drug Discovery,* 2, **2003**, pp. 205-213).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. {*In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)}.

The determination that *undue experimentation* would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. (*In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404). These factual considerations are discussed comprehensively in MPEP § 2164.08 (scope or breadth of the claims), § 2164.05(a) (nature of the invention and state of the prior art), § 2164.05(b) (level of one of ordinary skill), § 2164.03 (level of predictability in the art and amount of direction provided by the inventor), § 2164.02 (the existence of working examples) and

§ 2164.06 (quantity of experimentation needed to make or use the invention based on the content of the disclosure).

Based on a preponderance of the evidence presented herein, the conclusion that applicant is insufficiently enabled for making and a pharmaceutical composition for modulating the activities of peroxisome proliferator activated receptor gamma sub type, is clearly justified.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew P. Coughlin whose telephone number is (571)270-1311. The examiner can normally be reached on Monday through Thursday from 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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